REMARKS/ARGUMENTS

Claims 1 to 22 are pending in this application. In the Office Action, claims 6 to 22 are withdrawn from consideration and

(1) claims 1 to 5 are rejected under 35 U.S.C. § 112, second paragraph;

(2) claims 1 to 5 are rejected under 35 U.S.C. § 102(b) over US-A-5,461,146;

(3) claims 1 to 5 are rejected under 35 U.S.C. § 103(a) over US-A-5,461,146; and

(4) claims 1 to 5 are rejected under the judicially-created doctrine of obviousness-type double patenting over claims 1 to 4 of US-B-6,306,849.

Applicants are herein amending the specification, amending claims 1 and 5 and canceling claims 6 to 22, without prejudice or disclaimer. Upon entry of this amendment, claims 1 to 5 will be pending in this application.

Amendments

Applicants are herein amending the specification to update the cross-reference to related applications. Applicants are herein canceling claims 6 to 22, without prejudice or disclaimer. Applicants are herein amending claim 1 to present the preamble in a different form, to clarify that the moieties R^5 and R^6 and the moieties R^{23} and R^{24} may together form a heterocyclic ring with the nitrogen to which they are attached, and to eliminate hydrogen as an option for R^4 when R^1 or R^2 in formula I is $-CO(CH_2)_jR^4$. Applicants are herein amending claim 5 to delete a duplicate member in the Markush group. Applicants submit that the amendments to the specification and claims do not introduce new matter and are fully supported by the specification and claims, as originally filed.

Restriction Requirement

Restriction has been required under 35 U.S.C. § 121 between:

I. Claims 1 to 5, drawn to a compound of formula (I), classified in class 540, subclass 545.

II. Claims 6 to 11, drawn to a method for enhancing the function of a trophic factor responsive cell, comprising the step of contacting said cell with a compound of formula (I), classified in class 514, subclass 211.01.

III. Claims 12 to 16, drawn to a method for enhancing the survival of a trophic factor responsive cell, comprising the step of contacting said cell with a compound of formula (I), classified in class 514, subclass 211.01.

IV. Claims 17 to 22, drawn to a method for enhancing the survival of a cell at risk of dying, comprising the step of contacting said cell with a compound of formula (I), classified in class 514, subclass 211.01.

It is asserted that the inventions of Group I and Groups II to IV are related as product (Group I) and process of use (Groups II to IV). Applicants traverse the restriction requirement because there would be no serious burden in carrying out examination of all of the subject matter of the claimed invention in a single application.

According to MPEP § 803, there are two criteria for a proper requirement for restriction between patentably distinct inventions:

(A) The inventions must be independent (see MPEP § 802.01, § 806.04, § 808.01) or distinct as claimed (see MPEP § 806.05 to § 806.05(i)); and

(B) There must be a serious burden on the examiner if restriction is required (see MPEP § 803.02, § 806.04(a) to § 806.04(i), § 808.01(a), and § 808.02).

For purposes of the initial requirement, a serious burden may be *prima facie* shown if the examiner shows separate classification, separate status in the art, or a different field of search as defined in MPEP § 808.02. In the subject application, the claims have been restricted into four different groups, however, these groups have only been classified into two different classes, namely Class 540 and Class 514. At a minimum, applicants respectfully request reconsideration with respect to a reduction in the number of groups from four to two.

Nonetheless, to be fully responsive to the restriction requirement, applicants confirm the election of the subject matter of Group I, claims 1 to 5.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 1 to 5 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Applicants respectfully traverse the rejection because the pending claims are clear and definite, as amended.

(i) The Office Action alleges that the use of the preamble "A compound defined by the general formula (I)" is open-ended. Applicants submit that the preamble is not open-ended because it is stating that the compound may be defined by a generic formula. However, to expedite prosecution of the application, applicants are herein amending the preamble to state "A compound of formula (I)," as recommended in the Office Action, thus rendering the rejection moot.

(ii) The Office Action alleges that the term "substituted" as used in the claims is indefinite. Applicants respectfully submit that the term "substituted" is clearly defined in the specification and that one skilled in the art would understand the scope and meaning of the term as it is used in the claims. See, for example, page 7, lines 26 to 29, where the term "substituted" as it is used with respect to a "lower alkyl" group is defined to include one to three independently-selected substituents, such as hydroxy, lower alkoxy, carboxyl, lower alkoxycarbonyl, nitro, amino, mono- or di-lower alkylamino, dioxolane, dioxane, dithiolane, and dithione. See also, page 7, line 32 to page 8, line 2, where the term "substituted" as it is used with respect to "aryl," "heteroaryl," and "aralkyl" groups is defined to include one to three independently-selected substituents, such as lower alkyl, hydroxy, lower alkoxy, carboxy, lower alkoxycarbonyl, nitro, amino, mono- or di-lower alkylamino, and halogen.

(iii) The Office Action alleges that the term "heteroaryl" as used in the claims is indefinite. Applicants respectfully submit that the term "heteroaryl" is clearly defined in the

specification and that one skilled in the art would understand the scope and meaning of the term as it is used in the claims, including the number and type of heteroatoms present, ring size and number of rings. See, for example, page 7, lines 22 to 25 where the term "heteroaryl" moiety is defined to include at least one hetero atom selected from O, S, and N, and include pyridyl, pyrimidyl, pyrrolyl, furyl, thienyl, imidazolyl, triazolyl, tetrazolyl, quinolyl, isoquinolyl, benzoimidazolyl, thiazolyl and benzothiazolyl. Applicants submit that one skilled in the art would have no difficulty understanding what moieties are meant to be encompassed by the term as it is generally known in the art. See, for example, the definitions provided by the IUPAC (attached).

(iv) The Office Action alleges that the term "heterocyclic" and the definition of "R^5 and R^6" when combined are indefinite. Applicants are herein amending the definition of "R^5 and R^6" when combined to specify that they form a heterocyclic group along with the nitrogen to which they are attached. This amendment renders moot the rejection with respect to the combination. With respect to the term "heterocyclic," applicants submit that the term would be clear to one skilled in the art based on the possible limited number of cyclic arrangements of R^5 and R^6 when they are combined with the nitrogen atom to which they are attached, as required by amended claim 1.

(v) The Office Action alleges that the term "acyl" as used in the claims is indefinite. Applicants respectfully submit that the term "acyl" is clearly defined in the specification and that one skilled in the art would understand the scope and meaning of the term as it is used in the claims. See, for example, page 7, lines 17 to 20 where an "acyl" moiety is defined to include "a straight-chain or branched alkanoyl group having 1 to 6 carbon atoms, such as formyl, acetyl, propanoyl, butyryl, valeryl, pivaloyl and hexanoyl, an arylcarbonyl group described below, or a heteroarylcarbonyl group described below."

(vi) The Office Action alleges that the definition of "$NR^{23}R^{24}$" as "the residue of an α-amino acid in which the hydroxyl group of the carboxyl group is excluded" is unclear with respect to which amino acids are intended. The Office Action also alleges that the term "heterocyclic group" is not clear. With respect to the term "heterocyclic," applicants

respectfully submit that the term would be clear to one skilled in the art based on the possible limited number of cyclic arrangements of R^{23} and R^{24} when they are combined with the nitrogen atom to which they are attached, as required by amended claim 1. Applicants respectfully submit that it is clear what amino acids are intended by the phrase "the residue of an α-amino acid in which the hydroxyl group of the carboxyl group is excluded." In the specification on page 8, lines 7 to 9, applicants specify that the "α-amino acid" include glycine, alanine, proline, glutamic acid and lysine in L-form, D-form or a racemic mixture thereof. Thus, it would be clear to one skilled in the art the structure of one of these amino acids where the hydroxyl of the carboxy group is not present.

Applicants respectfully submit that the claims, as amended, are not indefinite and particularly point out and distinctly claim the subject matter that applicants regard as the invention. Thus, applicants respectfully request withdrawal of the rejection of pending claims under 35 U.S.C. § 112, second paragraph.

Rejections under 35 U.S.C. § 102(b)

Claims 1 to 5 are rejected under 35 U.S.C. § 102(b) as anticipated by US-A-5,461,146 (*Lewis*). Applicants are herein amending claim 1 to eliminate hydrogen as an option for R^4 when R^1 or R^2 in formula I is $-CO(CH_2)_jR^4$. Claim 1, as amended herein, requires that R^1 or R^2 be selected from:

a) $-CO(CH_2)_jR^4$;
b) $-CH(OH)(CH_2)_bR^{4A}$;
c) $-(CH_2)_dCHR^{31}CO_2R^{32}$;
d) $-(CH_2)_dCHR^{31}CONR^5R^6$;
e) $-(CH_2)_kR^7$;
f) $-CH=CH(CH2)_mR^{12}$;
g) $-CH-C(CO_2R^{33A})_2$;
h) $-C\equiv C(CH_2)_nR^{13}$; and
i) $-CH_2OR^{44}$.

The *Lewis* reference does not disclose any compounds that meet all of the requirements of claims 1 to 5, as amended. Thus, applicants submit that *Lewis* does not anticipate applicants' claimed invention. Accordingly, applicants request withdrawal of the rejection of claims 1 to 5 under 35 U.S.C. § 102(b).

Rejection under 35 U.S.C. § 103(a)

Claims 1 to 5 are rejected under 35 U.S.C. § 103(a) as obvious over US-A-5,461,146 (*Lewis*). Applicants respectfully traverse because *Lewis* does not disclose, teach or suggest the requisite elements of applicants' claimed invention, as defined in claims 1 to 5. Specifically, Lewis fails to disclose, teach or suggest any compounds where R^1 or R^2 is selected from:

a) $-CO(CH_2)_jR^4$;

b) $-CH(OH)(CH_2)_bR^{4A}$;

c) $-(CH_2)_dCHR^{31}CO_2R^{32}$;

d) $-(CH_2)_dCHR^{31}CONR^5R^6$;

e) $-(CH_2)_kR^7$;

f) $-CH=CH(CH2)_mR^{12}$;

g) $-CH-C(CO_2R^{33A})_2$;

h) $-C\equiv C(CH_2)_nR^{13}$; and

i) $-CH_2OR^{44}$.

With the exception of moiety (e) above, there is no evidence or reasoning presented in the Office Action of why any of the other R^1 or R^2 moieties would be obvious in view of the teaching of *Lewis*. There has been no evidence presented that would indicate the functional equivalence of the R^1 or R^2 moieties with those disclosed in *Lewis*, except allegedly with respect to moiety (e). With respect to moiety (e), it is alleged that the only difference between moiety (e) and the disclosure of Lewis is the length of the alkylene linker in $-(CH_2)_kR^7$. It is alleged that compounds II-3, II-47 and II-50, for example, only differ from the claimed compounds by virtue of a longer alkylene linker. However, applicants wish to point out that this in fact is not the case and that compounds II-3, II-47 and II-50 also differ in other respects:

Compound	R^1/R^2 moiety	Difference between R^1/R^2 of *Lewis* and R^1/R^2 of Claimed Invention
II-3	$CH_2SOC_2H_5$	R^1/R^2 moiety must be $-(CH_2)_kR^7$ where *k is 2 to 6* and no R^7 that is SOC_2H_5
II-47	$CH_2OC_2H_5$	In $-(CH_2)_kR^7$, *k is 2 to 6;* also in $-CH_2OR^{44}$, R^{44} must be a substituted lower alkyl
II-50	CH_2S-pyridinyl	In R^1/R^2 moiety, pyridinyl is not a possible substitution in $-(CH_2)_kR^7$ where R^7 is SR^{27}; *k is 2 to 6*

Applicants respectfully submit that the *Lewis* reference as a whole does not provide any suggestion of the desirability of doing what the inventor has done. "To support the conclusion that the claimed invention is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references." *Ex parte Clapp*, 227 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985). Homology involves close structural similarity which must be considered with all other relevant facts in determining the issue of obviousness. *In re Mills*, 281 F.2d 218, 126 USPQ 513 (CCPA 1960); *In re Wiechert*, 370 F.2d 927, 152 USPQ 247 (CCPA 1967). As expressed in MPEP § 2144.09, homology should not be automatically equated with *prima facie* obviousness because the claimed invention and the prior art must each be viewed "as a whole." *In re Langer*, 465 F.2d 896, 175 USPQ 169 (CCPA 1972) (Claims to a polymerization process using a sterically hindered amine were held unobvious over a similar prior art process because the prior art disclosed a large number of unhindered amines and only one sterically hindered amine (which differed from a claimed amine by 3 carbon atoms), and therefore the reference as a whole did not apprise the ordinary artisan of the significance of hindered amines as a class.).

Applicants respectfully submit with respect to moiety (e) of R^1/R^1 that the *Lewis* reference, viewed as a whole, does not disclose, teach or suggest to the ordinarily skilled

artisan the desirability of increasing the carbon length of the alkylene moiety. Applicants further respectfully submit with respect to the other compounds that *Lewis* does not expressly or impliedly suggest the claimed invention nor would a artisan find the claimed invention obvious in light of *Lewis*.

Thus, applicants respectfully submit that *Lewis* does not render obvious applicants' claimed invention. Accordingly, applicants request withdrawal of the rejection of claims 1 to 5 under 35 U.S.C. § 103(a).

Obviousness-Type Double Patenting Rejection

Claims 1 to 5 are rejected under the judicially-created doctrine of obviousness-type double patenting over claims 1 to 4 of US-B-6,306,849. Applicants request that this rejection be held in abeyance until the identification of allowable subject matter, at which time applicants will consider submitting a terminal disclaimer to obviate the rejection.

Conclusions

Applicants request:

(1) entry of the amendment to the specification and claims; and

(2) reconsideration and withdrawal of the rejection of the claims; and

(3) allowance of claims 1 to 5.

If the Examiner is of a contrary view, the Examiner is requested to contact the undersigned attorney at (215) 557-3861.

Respectfully submitted,

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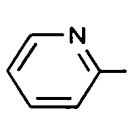
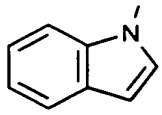
heterocyclic compounds
Cyclic compounds having as ring members atoms of at least two different elements, e.g. quinoline, 1,2-thiazole, bicyclo[3.3.1]tetrasiloxane.
See *homocyclic compounds, carbocyclic compounds.*
1995. *67*, 1340

heteroaryl groups
The class of *heterocyclyl groups* derived from *heteroarenes* by removal of a hydrogen atom from any ring atom; an alternative term is hetaryl. E.g.



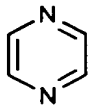
2-pyridyl (pyridin-2-yl)



indol-1-yl

1995, *67*, 1340

heteroarenes
Heterocyclic compounds formally derived from *arenes* by replacement of one or more methine (–C=) and/or vinylene (–CH=CH–) groups by trivalent or divalent heteroatoms, respectively, in such a way as to maintain the continuous π-electron system characteristic of aromatic systems and a number of out-of-plane π-electrons corresponding to the Hückel rule ($4n + 2$); an alternative term is hetarenes.



1995, *67*, 1340